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ORIGINAL ARTICLE

Role of carbon dioxide angiography in management of below knee arterial lesions

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KEYWORDS

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Abstract *Introduction:* Many practitioners express concern about the adequacy of imaging using CO2 in the lower extremities, particularly in the distribution of the popliteal artery and below (5). Published results have varied considerably with respect to the validity of imaging this anatomy.
Objectives: Review our experience with CO2 angiography using CO2 angioset in evaluation and intervention of below knee arteries.
Patients and methods: Forty patients with lower limb ischemia were divided into two groups. The 1st group has normal kidney function, subjected to angiography with CO2 and water soluble contrast media (WSCM) as the reference standard (control). The 2nd group has subjected only to CO2 angiography due to one or more risk factors related to WSCM. CO2 angioset is a dedicated CO2 injection system used in all patients. In the 1st group; imaging findings on CO2 and WSCM angiography were compared while in the 2nd group; findings were compared with the post procedure clinical and color Doppler findings.

Abbreviations: ATA, anterior tibial artery; CDS, color Doppler sonography; CLI, critical limb ischemia; CO_2, carbon dioxide; PA, popliteal artery; PCV, pressure chamber volume; PTA, posterior tibial artery; SFA, superficial femoral artery; TPT, tibioperoneal trunk; WSCM, water soluble contrast media

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Results: All arterial lesions detected on CO2 angiography were comparable to those obtained with WSCM in the control group. In the 2nd group; post procedure clinical and Doppler findings correlated well with angiographic findings and angioplasty results. CO2 angiography images have lower resolution compared to WSCM however, they were reliable for accurate diagnosis and to guide angioplasty.

Conclusion: CO2 angiography using CO2 angioset is considered a reliable alternate to WSCM in assessment of below knee arteries and provides a reliable roadmap to interventional procedures.

1. Introduction

Carbon dioxide is a nontoxic, compressible gas that has been used as a contrast agent since the early 1900s (1). As a contrast agent, CO_2 does not appear to carry the risks of either contrast nephropathy or allergic reaction (2). Since its implementation in the vascular system by Haskins in the 1970s, the use of CO_2 as a contrast agent has been validated in a number of studies (1). It has been found to be particularly advantageous in the treatment of renal artery stenosis and the endovascular management of infra-renal abdominal aortic aneurysms (3,4). Despite these encouraging results, the adoption of CO_2 as a contrast agent in the evaluation and treatment of lower extremity arterial disease has not been as pervasive as one might expect. There seem to be two primary reasons that contribute to this limitation. The use of a gas rather than a liquid contrast agent changes a number of elements in the process of angiography that may be unfamiliar to vascular interventional practitioners. Many practitioners express concern about the adequacy of imaging using CO_2 in the lower extremities, particularly in the distribution of the popliteal artery and below (5). Published results have varied considerably with respect to the validity of imaging this anatomy (6).

2. Aim of study

To present our experience with CO_2 angioset in performing diagnostic and interventional procedures in patients with lower limb ischemia with special emphasis on below knee arteries.

3. Patients and methods

This prospective study was approved by the institutional review board and informed consent was obtained from all patients. It included 40 patients done over a period of 8 months (from March through October 2011). All patients with symptoms and signs of lower limb ischemia were subjected to thorough clinical examination and color Doppler study. They were 22 males and 18 females, their age ranged from 45 to 84 years. Patients were divided into two groups, each group composed of 20 patients. Patients in the 1st group have normal kidney function, subjected to angiography with CO_2 then each series is repeated with WSCM as the reference standard (control group). The 2nd group subjected only to CO_2 angiography due to presence of one or more of indications described below. All studies were done in angiography suite (Siemens Axiom Artis) using CO_2 angioset (OptiMed). All procedures were done under local anesthesia (LA) except two patients done under general anesthesia (GA). Before the procedure; baseline vital signs (e.g., pulse and blood pressure) were recorded and echocardiographic findings (e.g., ejection fraction) were reviewed.

CO_2 angiography was indicated in patients with renal insufficiency especially those with borderline kidney function (serum creatinine 1.5–2.5 mg/dL), intolerance to iodinated WSCM (e.g., history of allergy), to reduce strain caused by WSCM (e.g., heart failure, low ejection fraction or complex interventional procedure), and hyperthyroidism.

CO_2 angiography passes through four steps: (1) an end-hole 4F or 5F diagnostic catheter or a 5F-6F sheath is advanced proximal to examined region e.g., PA or lower SFA to examine leg arteries, (2) preparation of CO_2 angioset which is a dedicated CO_2 injection system, (3) elevate patient's leg 15–20 degrees either by tilting the table or using a wedge-shaped cushion, (4) imaging.

CO_2 angioset is composed of a gas bottle containing pure medical CO_2 (99.7 vol.% or higher), pressure relief valve, sterile filter (optional but recommended to filter rust particles), 150 cm gas supply line with connection to the pressure relief valve, stop-cock with 90° rotary valve for loading and injection procedure, 100 ml syringe adjustable in 20 ml steps and connection tube to the patient which is 150 cm in length (Fig. 1A–D).

The set is prepared by removing the syringe from package; the locking plate is set to the desired volume. The gas supply line is connected to the outlet of pressure relieve valve of the gas bottle, the system is rinsed by turning the stop-cock back and forth five times holding the syringe vertically (CO_2 is heavier than air). After rinsing, the stop-cock is set to the loading position then; the connection tube is linked to the catheter or sheath hub or to the side limb of a rotating hemostasis valve if injection occurs with wire in place. The pressure must be set at 1.3 bars to avoid overdosage.

Regarding imaging; CO_2 setting is activated which utilizes special software required to image negative contrast media and the number of images should be increased to 4–6 per second. After starting the DSA series and preparing the mask images, injection is carried out by turning the stop-cock to the injection position. The stop-cock is returned to the loading position after completion. The CO_2 angioset is ready for the next DSA series.

Imaging of leg arteries is usually performed with 40–60 ml PCV. Generally we start with lower volume (40 ml PCV) and if acquired images are not satisfactory; the larger volume (60 ml PCV) is used. To avoid pain during injection, we start with lower volumes and wait at least 2 min between each series (longer for patients with pulmonary disease). In case of severe leg pains, the leg is positioned at lower level and 50–100 mg pethidine is injected intravenous. Nitroglycerin 100–300 μg is injected intra-arterial to enhance gas flow and filling of the dis-

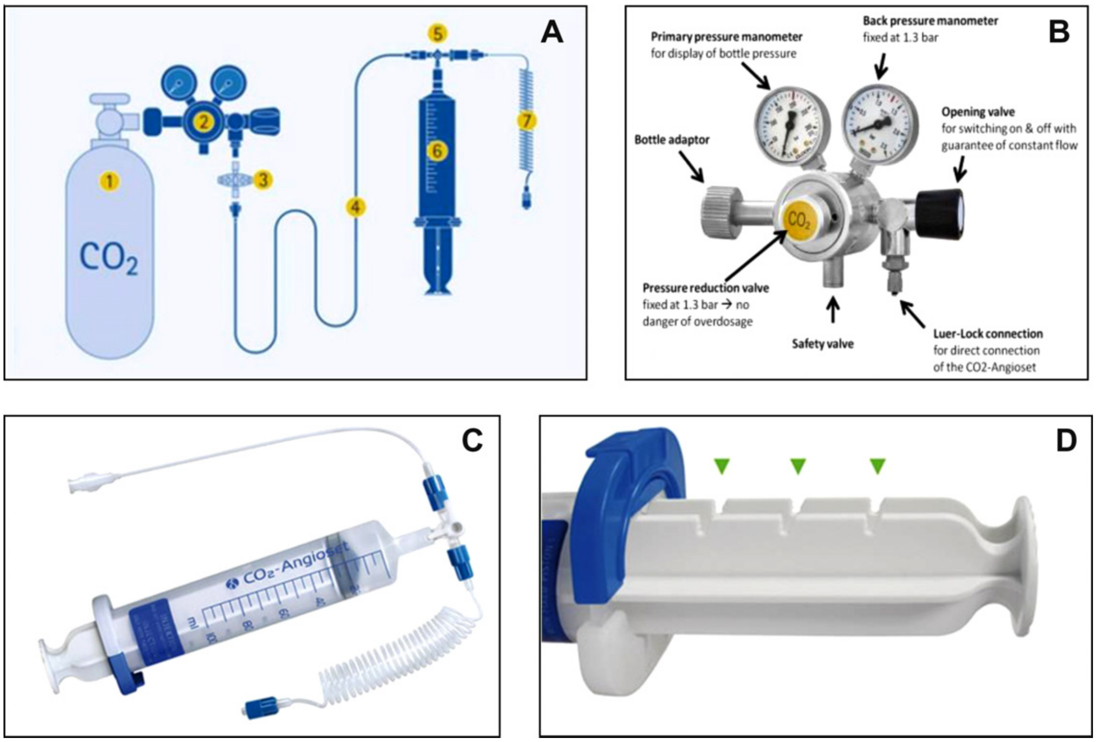

Fig. 1 Component and function of CO2 angioset. (1A) The set is composed of gas bottle containing pure medical CO2 (1), pressure relief valve (2), sterile filter (3), gas supply line with connection to the pressure relief valve (4), special stop-cock with 90° rotary valve (5), 100 ml syringe adjustable in 20 ml steps (6) and connection tube to the patient (7). (1B) Shows the component and functions of pressure relieve valve. (1C and D) Shows the syringe and plunger adjustable in 20 ml steps.

tal arteries. The blood pressure is carefully monitored during and after nitroglycerin injection.

Breaking of contrast column is noted in 16 cases. This was overcome by using post-processing stacking software.

4. Results

Regarding control group, all arterial lesions detected on CO_2 images were compared with that obtained with WSCM. Stenotic lesions were assessed regarding degree and length of stenosis and distal run-off was assessed as well. All lesions show similar findings on CO_2 and WSCM images (Figs. 2 and 3).

Regarding the 2nd group, diagnosis and angioplasty were based on CO_2 images alone. Post-angioplasty clinical and color Doppler findings correlated well with imaging findings and intervention procedure done (Figs. 4–6).

CO_2 injection was painless in 10 cases, pain was mild in 15, moderate but tolerable in 9 cases, severe intolerable in 4 cases that required administration of IV sedation (pethidine 50–100 mg). The 2 cases done under GA are excluded from pain response assessment. Nitrous oxide was not used as an anesthetic agent in these 2 cases.

5. Discussion

Carbon dioxide has been used as an arterial contrast agent since 1971. The development of digital subtraction angiography and an automated CO_2 injector has increased the practicability and safety of using CO_2 routinely (7). CO_2 angiography is not available in most centers and generally reserved for patients with history of contrast allergy or renal dysfunction with creatinine clearance less than 20 mL per minute. The use is generally limited to arteries below the diaphragm to minimize the risk of cerebral embolism. DSA equipment is required for CO_2 angiography (8).

CO_2 is a colorless and odorless gas, and it cannot be visually distinguished from air. The incorrect application of technique may result in air contamination, which may cause serious complications. CO_2 is approximately 20 times more soluble than oxygen. When injected into a vessel, CO_2 bubbles completely dissolve within 2–3 min. Two to 3 min should elapse between injections of CO_2 to prevent the localized accumulation and trapping of gas bubbles (9).

CO_2 is compressible during injection; it expands in the vessel as it exits the catheter. Clearing the fluid of the catheter by using 3–5 cc of CO_2 before injection reduces the explosive delivery. The explosive delivery is unlikely to cause vascular damage, but it may contribute to discomfort during the injection (9).

CO_2 is lighter than blood plasma; therefore, it floats above the blood (buoyancy). When injected into a large vessel such as the aorta or inferior vena cava, CO_2 bubbles flow along the anterior part of the vessel, with incomplete blood displacement along the posterior portion (9). The buoyancy is not a problem when the vessel to be imaged is smaller than 10 mm in diameter because the gas bubbles tend to displace the blood in greater than 80% of the lumen. Elevation of the lower extremity to 15–20° in conjunction with the intra-arterial injection of 100–

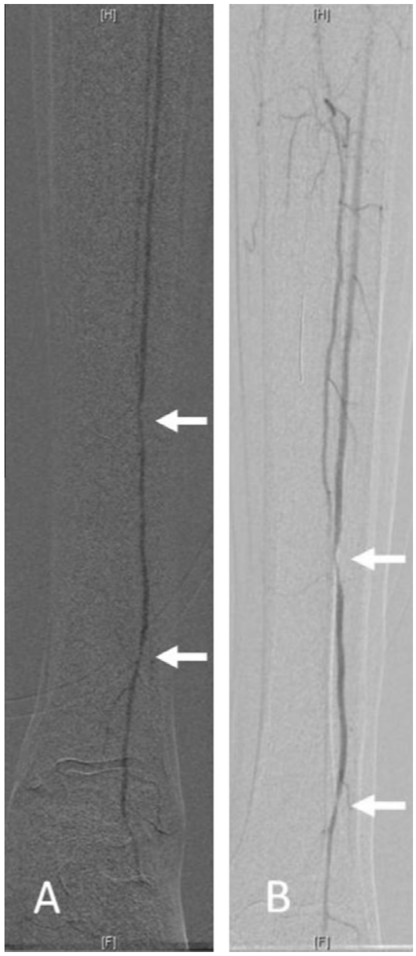

Fig. 2 Sixty-two YOM heavy smoker, DM, HTN presented with acute ischemia LT LL. (A) CO_2 angiography shows two stenotic segments in ATA (arrows), fading away of peroneal A and non opacified PTA. These findings correlated well with WSCM angiography (B).

200 μg of nitroglycerin enhances gas flow and filling of the distal arteries in the lower extremity.

CO_2 is approximately 400 times less viscous than iodinated contrast medium. The low viscosity permits manual gas injection with small-bore catheters between the catheter and guide wire, accounts for better filling of collateral vessels and allows detecting very narrow channel in segments that have apparent total occlusion with WCSM (9). Iodinated contrast medium mixes with blood when injected into a vessel and becomes diluted, making it less dense as it travels through collateral vessels. By contrast, CO_2 does not mix with blood, and so it does not become diluted by collateral flow.

CO_2 is less dense than WSCM and the overall quality of CO_2 images is slightly less than that obtained with WSCM. However, CO_2 has several advantages when compared with WSCM. CO_2 is a natural byproduct, so it does not cause allergic reaction. CO_2 causes no renal or hepatic toxicity. In addition, unlimited amounts of CO_2 may be used for vascular imaging because the gas is effectively eliminated by means of respiration. However, the operator should allow sufficient time for its clearance. A minimum of 2 min is needed for the first CO_2 dose to completely dissolve before another dose is injected. CO_2 is particularly useful for patients with compromised cardiac and renal function who are undergoing complex vascular interventions (9).

In the lower extremities, injection can sometimes give the patient a somewhat shocking feeling that may prompt movement and cause imaging degradation. Generally, patients are pre-informed about possibility of pain, they are instructed to keep limb stable and when necessary, limb is strained. Other helpful tips are to inject smaller volumes and to allow a period of time (2–3 min) for CO_2 clearance between injections. Pethidine 50–100 mg IV and lowering patient's leg may also help alleviate pain. In extreme cases in which a patient is likely to have difficulties remaining still during the procedure, general anesthesia may be an option. Once again, nitrous oxide should probably be avoided as an anesthetic agent in these cases.

Multiple studies have suggested that imaging with CO_2 is limited with respect to accuracy at the popliteal artery and

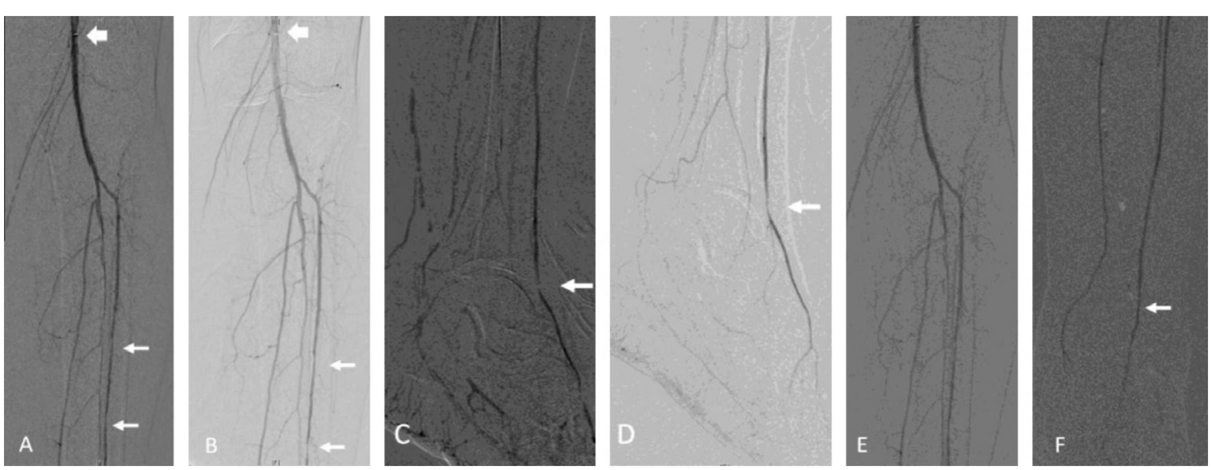

Fig. 3 Fifty-five YOM with foot ulcer and normal kidney function. Angiography with CO_2 (A and C) and WSCM (B and D) for leg arteries shows comparable results. (A and B) Focal stenotic segments in ATA (arrows), block arrow indicates catheter tip. (C and D) Focal stenotic segment in DPA. (E and F) CO_2 angiography after balloon angioplasty shows good results.

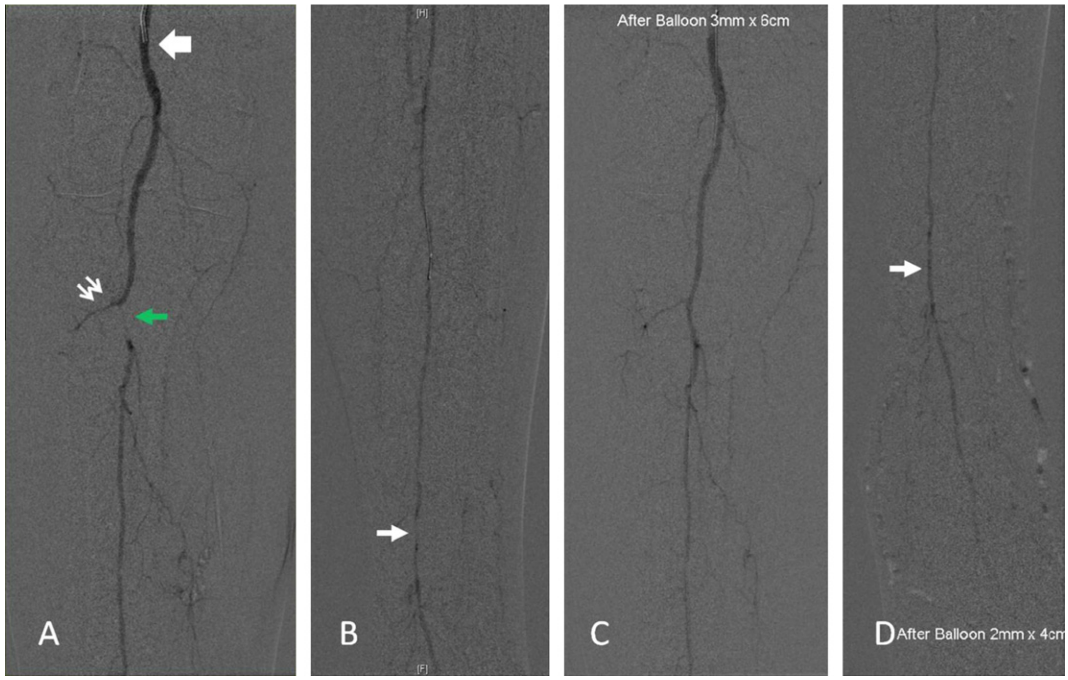

Fig. 4 Sixty-four YOF presented with RT CLI, serum creatinine = 1.8 mg/dL. (A and B) Diagnostic CO_2 angiography through 5F vertebral catheter in PA (block arrow) shows severe stenosis of TPT (green arrow), stenosis of proximal ATA (double arrows in A), total occlusion of distal ATA and all PTA. There is focal stenotic segment in distal peroneal A (arrow in B). DPA is opacified via anterior perforating branch. (C and D) Corresponding post-angioplasty for TPT and peroneal A shows good results.

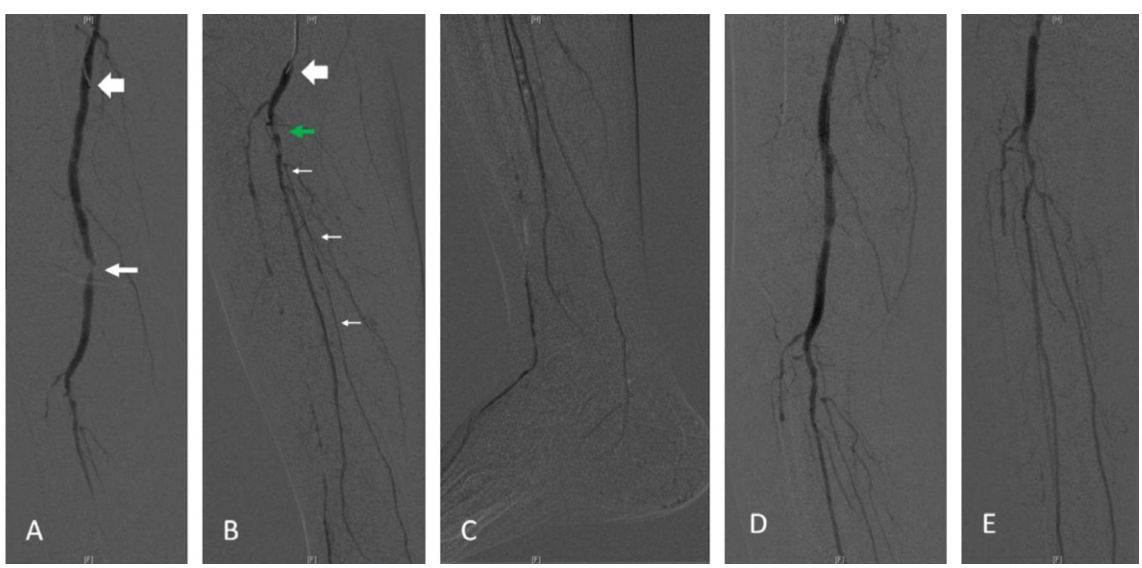

Fig. 5 Sixty-nine YOM with RT CLI and borderline kidney function for whom diagnosis (A, B and C) and intervention (D and E) done with CO_2 only. (A, B and C) Catheter tip indicated by block arrow, sever PA stenosis (arrow in A), TPT stenosis (green arrow in B), diffuse stenosis of proximal PTA (small arrows in C). The ATA shows alternating segments of stenosis and total occlusion however, there is refilling of distal ATA and DPA (B and C). (D and E) Post balloon angioplasty shows reconstruction of PA, TPT and PTA. ATA could not be recanalized.

below (1). In our study; we have founded CO_2 angiography using CO_2 angioset and DSA dedicated for CO_2 imaging are greatly helpful regarding diagnosis and intervention for leg and foot arteries. The diagnostic catheter or sheath should be advanced into lower SFA or popliteal artery, use of intra-arterial nitroglycerin and post-processing stacking help obtaining good quality images down to pedal arteries (Figs. 3 and 5).

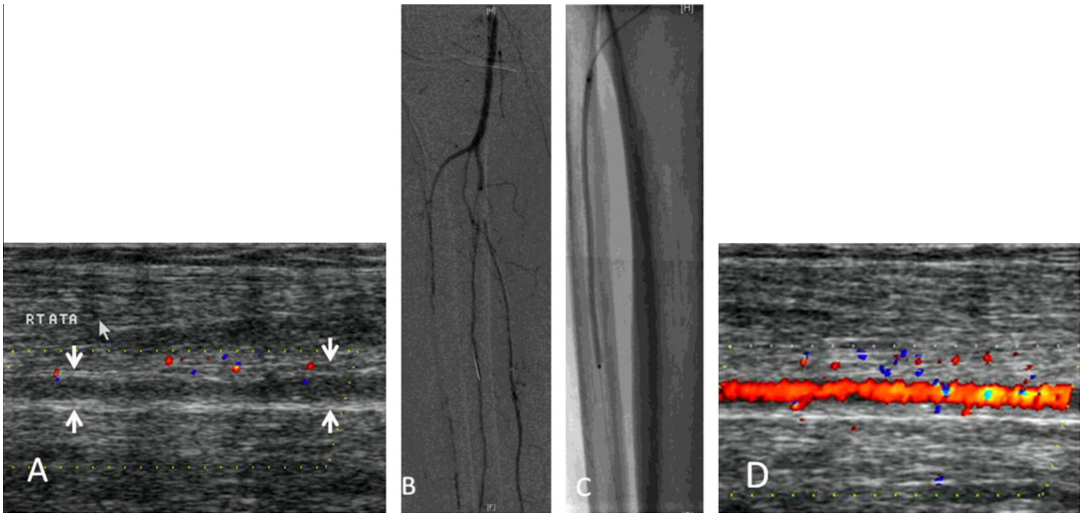

Fig. 6 Sixty-eight YOM with RT CLI and borderline kidney function. (A) Pre-procedure assessment with CDS shows absent flow signals in ATA (arrows), (B) CO_2 angiography confirmed ATA occlusion and also shows occlusion of distal TPT, (C) angioplasty with 2.5 mm plain balloon, (D) post procedure CDS proves recanalization of ATA. Whole procedure performed with CO_2 only.

6. Conclusion

CO_2 is a valuable alternative to traditional contrast agents for evaluating lower extremity arterial disease. The use of a dedicated injection system provides adequate delivery and avoids overdose and contamination. Although iodinated contrast agents still demonstrate superior imaging compared to CO_2, particularly in smaller vessels yet, CO_2 as a contrast agent provides good quality imaging required for reliable diagnosis and intervention in below knee arteries.

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